CONSANGUINITY AND RISK OF CONGENITAL DEFECTS- A SYSTEMATIC REVIEW

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ABSTRACT

BACKGROUND

Consanguineous unions are associated with an increased susceptibility to various forms of autosomal recessive inherited disease. The role of consanguinity in causation of congenital defects is not clear, as various genetic as well as environmental/epigenetic factors are involved in their aetiology.

In this study, we analysed the effect of consanguinity as a risk factor in occurrence of congenital defects.

MATERIALS AND METHODS

Systematically reviewed recent and past studies with different designs, methodologies conducted in different regions of world on the same subject and compared their conclusions. The reasons and incidence of consanguineous unions, types of consanguineous unions were assessed.

Settings and Design- ESIC Medical, Gulbarga, Department of Anatomy, Systematic Review Article.

RESULTS

Almost all studies support the view that congenital defects occur commonly in consanguineous couples than non-consanguineous couples, but the study designs varied significantly.

CONCLUSION

Congenital malformations occur more commonly in consanguineous couples than non-consanguineous couples with first cousins being the commonest type. The available articles have inadequately studied the actual (genetic) role of consanguinity in causation of congenital anomalies with multifactorial aetiology. There is a need of large population-based studies determining influence of consanguinity on occurrence of chromosomal abnormalities, thereby resulting in congenital anomalies.

KEY WORDS

Consanguinity, Congenital Defects, Congenital Malformations, Consanguineous Unions, Risk Factors, Genetics, Environment, Genetic Counselling


BACKGROUND

Consanguineous unions lead to the descent of autosomal recessive genes inherited from the common ancestors of either of the child-bearing couples, potentially leading to disease depending on the prevalence of consanguineous unions and the genetic contribution to disease.1 Many congenital defects have a genetic component in its causation, hence consanguinity may prove as a risk factor, particularly since prevalence of consanguinity has reached over 50% in some areas of the world and in some populations.2 A consanguineous marriage is defined as union contracted between persons/couple biologically related as second cousins or closer.3 The purpose of this article is to determine the role of consanguinity as a risk factor for occurrence of congenital defects.

Hence, it is the responsibility of health care providers to care for families involved in consanguineous unions and discuss and manage potential health concerns in an appropriate manner.4 Despite the complexity in the aetiology of various congenital malformations consanguinity can act as a risk factor for its occurrence, particularly if the disease has a recessive or multifactorial inheritance pattern. This possibility has been explored by a number of groups, who have attempted to quantify the potential degree of increased risk. However, these studies have varied in their scope, design and analysis, and as a result, different conclusions were drawn. For this review, we performed a detailed analysis of recent and old published articles addressing consanguinity and congenital defects.

MATERIALS AND METHODS

We searched for all articles from MEDLINE, PUBMED (January 1958 - December 2017) using the Medical Subject Headings (MeSH) terms “Congenital defects, congenital malformations” and “consanguinity” limited to the English language, which yielded more than 100 articles. We focused on articles that studied effect of consanguinity on congenital defects and its correlation with parental age, education, occupation, intra/extrauterine mortality, parity, religion and we could shortlist 94 such original articles which matched our study directly or indirectly.

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Sl. No. | Subject of the Article | No. of Studies
--- | --- | ---
1. | Consanguinity and its effects on child growth | 1
2. | Consanguinity and its effects on congenital defects | 45
3. | Consanguinity and its effects on anthropometric parameters of child | 15
4. | Correlation of parental age with occurrence of consanguineous marriages | 14
5. | Correlation of parental education with occurrence of consanguineous marriages | 12
6. | Correlation of parental occupation with occurrence of consanguineous marriages | 6
7. | Correlation of parity/ fertility with occurrence of consanguineous marriages | 15
8. | Effect of consanguinity on incidence of intra/extrauterine loss (stillbirths, neonatal deaths etc.). | 31
9. | Effect of Inbreeding on increase variance of tooth diameter | 1
10. | Correlation of religion with occurrence of consanguineous marriages | 4

Table 1. We classified these 94 articles accordingly in Table 1

Following Inclusion Criteria were used to Further Shortlist these 94 Studies for this Review Article:
1. Cross-sectional and longitudinal studies preferably retrospective studies were considered.
2. Studies conducted in regions among participants affected by radiation exposure, nuclear or bomb explosions or any other source responsible for congenital malformations were excluded.
3. Research articles who had studied the same objectives which were studied by the author in his own original study and this review article were only considered to keep the discussion precise.

Amongst shortlisted 94 articles, 16 articles were selected as they were conducted with adequate sample size which gave statistically significant findings. Research articles studying too many variables were rejected. These 16 original research articles matched author’s own study in design, analysis and objectives studied:
- Total number of articles found: 94
- Total number of articles shortlisted: 16
- Total number of articles rejected: 1
- Statistical tests/methods used: Nil

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Sl. No. | Author | Reason for Rejection
--- | --- | ---
1. | William Schull 1958 | Results in this study were influenced by atomic explosions in Hiroshima and Nagasaki regions

Table 2. Study that fulfilled the selection criteria but was Rejected

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RESULTS

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Authors</th>
<th>Database</th>
<th>Sample Selection Method / Type of Study</th>
<th>Incidence of Consanguineous marriages</th>
<th>Type of Consanguinity</th>
<th>Religion</th>
<th>correlation with Parental Education</th>
<th>Incidence of Children with Congenital Anomaly</th>
<th>Correlation with Parental Occupation</th>
</tr>
</thead>
</table>
1. | Ranajit Chakraborty, Aravinda Chakravarti | Book- Human Genetics, 05.01.1977, Vol. 36, Issue 1, 47-54 | Cross-sectional study-39,495 single birth records were analysed, India | Not stated | Not stated | Not stated | Not stated | Increased incidence in consanguineous group than non-consanguineous group | Not stated |
2. | Naderi S | PubMed-Medline- 1979 | Cross-sectional study-9623 newborns in Iran | Not stated | Not stated | Not stated | Not stated | Increased incidence in consanguineous group than non-consanguineous group | Not stated |
3. | PSS Rao and SG Inbaraj | Google scholar-1980 | Prospective/ Cross-sectional study in India | Not stated | No significant differences found in both the groups | Not stated | Not stated | No significant differences were found in incidence of cong. defects between both the groups | Not stated |
<table>
<thead>
<tr>
<th></th>
<th>Authors</th>
<th>Journal/Database</th>
<th>Study Design/Location</th>
<th>Incidence</th>
<th>Consanguinity</th>
<th>First Cousins</th>
<th>Additional Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Asha Bai PV, John TI et al</td>
<td>PubMed-Medline-1981</td>
<td>Case control study in India                                                          41.4%</td>
<td>Not stated</td>
<td>More common in Hindus</td>
<td>Not stated</td>
<td>Increased incidence in consanguineous group than non-consanguineous group</td>
</tr>
<tr>
<td>5</td>
<td>ML Kulkarni, Mathew Kurian</td>
<td>PMC, US National Library of Medicine-1990</td>
<td>Prospective cross-sectional study involving 3700 live and stillbirths at 3 hospitals in India 26.5%</td>
<td>Uncle-niece union most common than first cousins</td>
<td>More common in Hindus</td>
<td>Not stated</td>
<td>Significant increase in incidence in consanguineous group than non-consanguineous group</td>
</tr>
<tr>
<td>6</td>
<td>VK Jain et al</td>
<td>PubMed-Medline-1993</td>
<td>Case control study done in JIPMER, India                                             41.4%</td>
<td>Not stated</td>
<td>First cousins, 50.6%</td>
<td>Not stated</td>
<td>Significant increase in incidence in consanguineous group than non-consanguineous group</td>
</tr>
<tr>
<td>7</td>
<td>Camilla Stoltenberg et al</td>
<td>PubMed-Medline-1996</td>
<td>Retrospective cross-sectional study in 1,566,839 birth records from Medical Birth Registry, Norway from 1967-1993 Not stated</td>
<td>No clear result</td>
<td>Pakistani population had higher incidence</td>
<td>Low parental education is associated with increased risk of birth defects</td>
<td>Low parental socio-economic status is associated with increased risk of birth defects</td>
</tr>
<tr>
<td>8</td>
<td>Badaruddoza Mohd. Afzal et al</td>
<td>PubMed-1998</td>
<td>Prospective cross-sectional study in 1672 singleton consecutive births in JNMC, Aligarb, India 37.98%</td>
<td>First cousins</td>
<td>Muslims</td>
<td>Negligible</td>
<td>Significant increase in incidence in consanguineous group than non-consanguineous group</td>
</tr>
<tr>
<td>9</td>
<td>Rittler M, Castilla EE</td>
<td>PubMed-Medline-2001</td>
<td>Case-control study in Latin-US                                                       36%</td>
<td>Not stated</td>
<td>Not stated</td>
<td>Not stated</td>
<td>Significant association of consanguinity and congenital anomalies was found</td>
</tr>
<tr>
<td>10</td>
<td>A Nath, C Patil et al</td>
<td>Medind.nic.in/researchgate.net-2004</td>
<td>Prospective cross-sectional study in India                                             36%</td>
<td>First cousins, 54.4%</td>
<td>Muslims &gt; Hindus</td>
<td>Not studied</td>
<td>Non-significant increase in incidence in consanguineous group than non-consanguineous group</td>
</tr>
<tr>
<td>11</td>
<td>Yunis K, Muntaz G et al</td>
<td>PubMed-Medline-2006</td>
<td>Case control study, Lebanon                                                           36%</td>
<td>Not stated</td>
<td>Not stated</td>
<td>Not stated</td>
<td>Significant increase in incidence in consanguineous group than non-consanguineous group</td>
</tr>
<tr>
<td>12</td>
<td>Z Mosayebi et al</td>
<td>PubMed-Medline-2007</td>
<td>Prospective study, Iran                                                               36%</td>
<td>Not stated</td>
<td>Not stated</td>
<td>Not stated</td>
<td>Significant increase in incidence of cong. defects in consanguineous group than non-consanguineous group</td>
</tr>
<tr>
<td>No.</td>
<td>Author(s)</td>
<td>Journal/ Source</td>
<td>Year</td>
<td>Study Design</td>
<td>Consanguinity Rate</td>
<td>First Cousin &gt; Uncle-Niece</td>
<td>Significant Association of Consanguinity</td>
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<tr>
<td>13</td>
<td>Sayee Rajangam, Rema Devi</td>
<td>Med India - 2007</td>
<td>Retrospective study done on 1376 individuals in South India</td>
<td>29.94%</td>
<td>First cousin &gt; uncle-niece</td>
<td>Not studied</td>
<td>Not studied</td>
</tr>
<tr>
<td>14</td>
<td>Khalid Yunis MD, Reem El Rafei et al</td>
<td>Neo reviews-2008</td>
<td>Review study in Lebanon</td>
<td>Not stated</td>
<td>First cousins</td>
<td>Not stated</td>
<td>Not stated</td>
</tr>
<tr>
<td>15</td>
<td>Naeimeb Tayebi et al</td>
<td>PMC, US National Library of Medicine-2010</td>
<td>Descriptive cross-sectional study in Iran</td>
<td>25%</td>
<td>First cousins</td>
<td>Not studied</td>
<td>Not studied</td>
</tr>
<tr>
<td>16</td>
<td>AL-Kandari YY, Crews DE</td>
<td>PubMed-Medline-2011</td>
<td>Cross-sectional study in Kuwait</td>
<td>Not stated</td>
<td>First cousins</td>
<td>Not studied</td>
<td>Not studied</td>
</tr>
</tbody>
</table>

Table 3. Research Articles included for this review that Fulfilled Selection Criteria

Effect of Consanguinity on Congenital Defects Studied through Cross-Sectional/Longitudinal Studies

Ranjit Chakraborty and A Chakravarti in their study analysed 39,495 single birth records from Mumbai under WHO survey and found that the incidence of major malformations is significantly higher among the inbred offspring (1.34%) as compared to that among non-inbred ones (0.81%). The inbreeding effect on perinatal mortality (stillbirths and mortality during the first few days of life) is also found to be significant.

Naderi S studied 9526 consecutive pregnancies as well as resulting in 9623 new-borns. There were 7261 new-borns from non-consanguineous parents and 2362 (24.5%) babies from consanguineous marriages. The incidence of congenital abnormalities in new-borns of non-consanguineous parents was 1.66% as compared to 4.02% for new-borns of the consanguineous group. Major and multiple malformations were found to be slightly more common in the Consanguineous group. Prematurity, prenatal mortality rate and congenital abnormalities were more common in the consanguineous group.

Probably the closer the familial relationship of the parents, the greater the chances of congenital abnormalities.

PSS Rao, SG Inbaraj studied pregnancies of over 20,000 married women from rural and urban samples in North Arcot district were identified and investigated to study the effects of inbreeding like incidence of congenital anomalies, length of gestation and body measurements. No significant differences existed in the incidence of congenital anomalies among offsprings between the consanguineous and non-consanguineous marriages in the rural or in the urban area. Neither were any significant trends seen by degree of consanguinity or by birth order or by the different age groups. The types of malformations and their frequency seen in the consanguineous and non-consanguineous groups were similar. It is suggested that long-term inbreeding does not lead to appreciable effects on foetal growth and development.

ML Kulkarni and Matthees Kurian studied a total of 3700 consecutive live and stillbirths taking place at three hospitals between November 1985 and March 1987 and found that total of 26-5% of the total births in the present study were to consanguineous couples. The Hindus had a consanguinity rate of 28 - 1%, while the Moslems had a consanguinity rate of 21.3%. Uncle-niece marriage was the most common form of mating 14.5% followed by first cousin marriage 10.1%. The frequency of malformations of major systems in consanguineous couples was significantly higher in our study.
These findings were matched with WHO collaborative study 23 conducted at 24 centres in 1966.

Camilla Stoltenberg et al.13 1996 in their study estimated the effects of consanguinity after adjusting for socioeconomic factors, maternal age, parity, year and place of birth. There was a two-fold increase in the proportion of children with birth defects among first-cousin parents in all groups considered. The risk of birth defects was higher in the Pakistani population as a whole compared with the other groups. This difference is explained by the high frequency of consanguineous marriages in the Pakistani population. Negative relation was found between parental educational levels and frequency of consanguinity. Similar findings have been demonstrated in previous studies.6,8,24,25

Badaruddoza Mohd. Afzal et al.14 1998 studied a total of 1672 singleton consecutive births in JNMC, Aligarh and found the incidence of congenital malformations among the consanguineous being significantly higher than that among the non-consanguineous marriages. First cousins were the most common consanguineous union.

AK Nath et al.15 in a study conducted in Shindoli village amongst resident married women (500) found that the frequency of consanguinity was 36%, which is less than that observed in other studies in South India.26-28 This could be attributed to the increasing modernisation, due to which the chances of such marriages are on the decline. Muslims showed a higher frequency of consanguinity as compared to Hindus. This finding is in contrast to that found in other studies, wherein consanguineous marriages were more among the Hindus. The most frequent type of consanguineous marriage was between first cousins (54.44%). Foetal losses before 28 weeks were higher in consanguineous group as compared to non-consanguineous group. The study, however, did not show a significant difference in the number of congenital malformations between the consanguineous and non-consanguineous groups.

Z Mosayabi16 2007 in his study determined the types, patterns and prevalence of congenital malformation among the offspring of consanguineous and non-consanguineous parents. In this prospective study of 3529 neonates delivered alive during a 1-year period, 109 had congenital malformations (3.09/1000 live births). The rate of congenital malformation was 2.0% among neonates from non-consanguineous marriages and 7.0% from consanguineous marriages. The most common malformations were genitourinary (32.1%), musculoskeletal (22.0%) and cardiovascular (14.7%). Of the total malformed infants, 8.3% died within the neonatal period. Male infants were at greater risk for birth malformations. A history of congenital malformation was more common in siblings of consanguineous than non-consanguineous marriages.

Sayee Rajamgam, Rema Devi17 in their retrospective study done by collecting information from 1376 individuals with MR and/or MCA stated that consanguinity seemed to have a significant association with MR and/or MCA. Consanguinity is considered to be an aetiological factor for increased occurrence of MCA and the subsequent morbidity/mortality. These findings were supported by Bromilaw et al.18 2004 Naderi S8 1979, Anand et al.19 1998, Bittles20 2001, Bittles21 2002 and Stevenson22 1966.

Nayemi Tayebi et al.21 in 2010 in a descriptive, cross-sectional study with consecutive sampling of new-born babies, who had been delivered at Shahid-Sadoughi Hospital, Yazd, Iran during a 9 months period from April to December 2008 found that the frequency of malformations in this study was higher compared with other studies which have been conducted in Iran. This may be due to industrial pollution. In this study, the gender of the foetus did not affect the prevalence of CM and both genders were equally distributed. The prevalence of anomalies was higher in consanguineous marriages than non-consanguineous marriages.

AL-Khandari YY22 studied a total of 9104 married Kuwaiti females aged 15 - 79 years from different backgrounds selected at ten primary health care centres from six governorates in Kuwait and stated that significant differences were found in the occurrence of genetic diseases in consanguineous couples’ offspring (4.88%) compared with those of non-consanguineous couples (4.13%). The results also show significant differences in frequencies of genetic/environmental diseases in consanguineous couples’ offspring (8.59%) compared with those of non-consanguineous couples (8.23%). A higher frequency of genetic diseases was found in first 6.97%, second 6.78% and third-cousin 6.46% couples offspring compared with those of non-consanguineous couples. The frequency of congenital disabilities in the offspring of couples from consanguineous marriages (2.9%) is higher than that in the offspring of non-consanguineous marriages (2.3%). First-cousin marriages have the highest frequency (3.5%) of congenital disabilities compared with other kinds of marriages (2.1 - 2.3%).

**Consanguinity in Congenital Defects Studied through Case Control Studies**

Asha Bai PV et al.23 studied 156 consanguineous marriages in comparison with 221 non-consanguineous marriages and found that developmental anomalies were significantly more frequent among the offspring of consanguineous parents. Among the 377 marriages, 156 (41.4%) were consanguineous and 221 (58.6%) were non-consanguineous. Consanguinity was more prevalent among Hindus than among Muslims or Christians. The frequency of developmental anomalies was significantly more frequent among the children of consanguineous parents.

VK Jain et al.22 in his study undertaken in JIPMER, Pondicherry, South India, wherein four hundred children with existing congenital developmental disorders were studied with regard to their consanguineous parentage and compared with 1,000 randomly selected patients attending the paediatric outpatient department. There was a significantly higher prevalence of consanguinity in the study group. The common type of consanguineous marriages was first cousins (50.6%). The frequency of consanguinity was significantly higher, especially with autosomal recessive disorders (p < 0.001), congenital heart diseases (p < 0.001), multiple malformations (p < 0.001), neurological malformations (p < 0.005), chromosomal disorders (p < 0.01), genitourinary disorders (p < 0.02) and mental retardation-developmental disorders (p < 0.02).

Castilla EE and Rittler15 in 2001 in their study observed a significant association with parental consanguinity for three congenital anomaly types: hydrocephalus, postaxial hand polydactyly and bilateral cleft lip +/- cleft palate, while three additional anomalies namely cephalocele, microcephaly and hand + foot postaxial polydactyly showed a positive association.
Yunis K and Muntaz G\textsuperscript{17} in 2006 in their case-control trial studied 173 new-borns having one or more congenital heart disease admitted to the Neonatal Intensive Care Units of participating hospitals during 3-year period from January 1, 2000 to December 31, 2002 and compared them with controls consisting of a random sample of 865 new-borns without a congenital heart disease admitted to the NICU during the same period and found that first cousin consanguinity is significantly associated with an increased risk of congenital heart disease. Infants born to first cousin marriages had a 1.8 times higher risk of having a congenital heart disease diagnosed at birth compared to those born to unrelated parents.

**Effect of Consanguinity on Congenital Defects Studied through Review Studies**

Khalid Yunis, Reem SL Rafel\textsuperscript{20} in 2008 in their review article stated that all studies reviewed showed a significantly higher rate of consanguinity was found in new-borns who had congenital anomalies compared with the general population. Also stated that most common form of consanguineous union was between first cousins, i.e. third-degree relationship.

**DISCUSSION**

The majority of studies support a relationship between consanguineous parentage and congenital defects (Table 3). Many studies used cross-sectional as well as case control designs and included cases of congenital defects diagnosed by methods such as ultrasonography records, interviewing the mothers etc. The analyses of cases and controls hence are critical. A few important points should be considered. First to what extent could confounding play a role in differences between case and control groups? Could the choice of certain cases and controls inadvertently lead to elevated or deflated effect sizes that are attributed to consanguinity? Many of these studies use controls from the same hospital or from the same geographic region as the cases to minimise potential confounders. Second, how was consanguinity defined and determined?

Most studies determined consanguinity and classified it as first and second cousin unions, although some studies failed to indicate how consanguinity had been defined. The history of consanguinity and other information related to type of congenital defect, parental education, occupation, religion, birth order etc. relied largely on the report by the parent of a child with congenital defect collected through questionnaire. There are increased chances of reporting bias or recall bias, which can affect the conclusions.

In PSS Rao, SG Inbaraj\textsuperscript{9} study, lay women interviewers fluent in local language with some training were employed for collecting information and identifying congenital malformations in new-borns. Chances of errors in identifying and categorising congenital defects from such interviewers cannot be ruled out. In A Nath et al\textsuperscript{16} study, type of personnel employed for interviewing women for data collection were not mentioned. Such data received from women participant cannot be error free. How consanguinity was defined and determined also was not described in this study. Similarly, in studies by AL-Kandari YY, et al\textsuperscript{22} in 2011 and Asha Bai PV et al\textsuperscript{10} 1981 data was collected using questionnaires from mothers. Sayee Rajangam, Rema Devi\textsuperscript{19} in their study collected data from available information on 1376 individuals with MR and/ or MCA. It was not clearly described how consanguinity was defined and determined and how congenital defects were classified.

Ranjit Chakraborty, A Chakravarti\textsuperscript{7} 1977, Naderi S\textsuperscript{8} in 1979, ML Kulkarni et al\textsuperscript{11} in 1990, VK Jain et al\textsuperscript{12} in 1993, Camilla Stoltenberg et al\textsuperscript{13} in 1996, Badaruldoza Mohd. Afzal et al\textsuperscript{14} 1998, Yunis K, Muntaz G et al\textsuperscript{17} 2006, Z Mosayebi et al\textsuperscript{18} in 2007, Naeimeb Tayebi et al\textsuperscript{23} in 2010, Rittler M and Castilla EE\textsuperscript{15} in 2001 in their studies collected data from hospital medical records, medical birth register which was recorded and maintained by medical personnel. Conclusions of such studies were more assuring.

Almost all the studies reviewed agreed and supported the point that congenital malformations were occurring more commonly in consanguineous couples than non-consanguineous couples except PSS Rao, SG Inbaraj\textsuperscript{9} 1980. Many studies\textsuperscript{8,19,29,30,31,32} agreed that consanguinity has a significant association with congenital defects, but its effect on congenital anomalies was non-significant. Congenital anomalies have diverse causes, the level of involvement of genetic component in its causation varies and is reflected by observed association of consanguinity with some anomalies, e.g. positive association was found between first cousin marriage and septic defects,\textsuperscript{17,33,34,35,36} but the risk of transposition of great vessels and of coarctation of the aorta was not significantly increased with consanguinity.\textsuperscript{17,33,35}

What about other minor congenital heart defects? Population-based studies that capture large number of lesions and that quantify relatedness will be helpful.\textsuperscript{37} Counselling in families with consanguinity and congenital anomalies is often performed. In absence of recognisable pattern of disease inheritance, families are presented with an empiric risk for congenital anomalies based on population data that may or may not consider the type of lesion. This risk may be modified depending on the individual family history and other clinical risk indicators and may be further adjusted due to the presence of consanguinity, although the degree of risk used in counselling has been variable.\textsuperscript{38} Based on our review of these articles, we recognise that future large population-based studies of birth defects should incorporate measures of genetic relatedness into their assessment and analysis, and recurrence of disease should be tracked. We still need to strive to understand the relative contribution of genetics versus the environment in congenital defects. If we can determine the proportional effect of consanguinity on disease, this may help determine the genetic contribution to a specific complex condition or the comparative role of genetics versus environmental influences.

Formation of a better understanding of the relationship between consanguinity and congenital anomalies will help to implement more accurate genetic counselling and more effective clinical management. We provide following suggestions: (1) Patients involved in consanguineous unions, should be aware of potential health risks and should assess them based on background population risk, effect of consanguinity, relevant family history and clinical assessment. They should not refer only to the data presented in the literature, for calculating magnitude of health risks instead should take the individual medical history and other potential indicators of that disease in consideration. (2) Healthcare providers and patients should be continuously trained about the importance of the medical family history.
while dealing with congenital anomalies. (3) Focus on prevention of diseases rather than its management. (4) Genetic predispositions to any disease should be investigated thoroughly. (5) The issue of consanguinity and consanguineous unions should be treated as a global health issue.

**CONCLUSION**

- Congenital malformations occur more commonly in consanguineous couples than non-consanguineous couples.
- First cousins are the commonest type of consanguineous unions occurring all over the world.
- Consanguinity has a significant association with congenital defects, but its effect on congenital anomalies as genetic aetiology is non-significant.
- The available articles have inadequately studied the actual (genetic) role of consanguinity in causation of congenital anomalies with multifactorial aetiology.
- There is a need of large population based studies determining influence of consanguinity on occurrence of chromosomal abnormalities, thereby resulting in congenital anomalies.

**REFERENCES**


